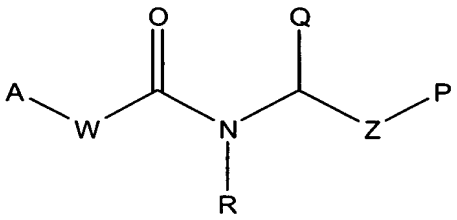
AMENDMENTS TO THE CLAIMS

1. (Currently amended) A pharmaceutical composition comprising a compound of Formula I,



(I)

wherein

A is a MetAP-2 inhibitory core;

W is O or NR;

each R is, independently, hydrogen or alkyl;

Z is –C(O)- or -alkylene-C(O)-;

P is NHR, OR or a peptide consisting of one to about one hundred amino acid residues connected at the N-terminus to Z;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is –OR, Q is not hydrogen;

or

Z is –alkylene-O- or –alkylene-N(R)-;

P is hydrogen or a peptide consisting of from one to about one hundred amino acid residues connected to Z at the carboxyl terminus;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is hydrogen, Q is not hydrogen;

or a pharmaceutically acceptable salts thereof,

and a pharmaceutically acceptable carrier.

2. (Currently amended) The pharmaceutical composition of Claim 1 wherein ~~Z is~~ Z is –C(O)- or C_1-C_4-alkylene-C(O)-.

3. (Previously Presented) The pharmaceutical composition of Claim 2 wherein Z is -C(O)- or C_1-C_2-alkylene-C(O)-.

4. (Previously Presented) The pharmaceutical composition of Claim 2 wherein Q is linear, branched or cyclic C_1-C_6-alkyl, phenyl or naphthyl.

5. (Previously Presented) The pharmaceutical composition of Claim 4 wherein Q is isopropyl, phenyl or cyclohexyl.

6. (Previously Presented) The pharmaceutical composition of Claim 1 wherein Z is C_1-C_6-alkylene-O- or C_1-C_6-alkylene-NR-.

7. (Previously Presented) The pharmaceutical composition of Claim 6 wherein Z is C_1-C_4-alkylene-O- or C_1-C_4-alkylene-NH-.

8. (Previously Presented) The pharmaceutical composition of Claim 7 wherein Z is C_1-C_2-alkylene-O- or C_1-C_2-alkylene-NH.

9. (Previously Presented) The pharmaceutical composition of Claim 6 wherein Q is linear, branched or cyclic C_1-C_6-alkyl , phenyl or naphthyl.

10. (Previously Presented) The pharmaceutical composition of Claim 9 wherein Q is isopropyl, phenyl or cyclohexyl.

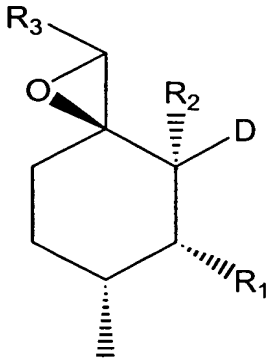
11. (Previously Presented) The pharmaceutical composition of Claim 1 wherein each R is, independently, hydrogen or linear, branched or cyclic C_1-C_6-alkyl.

12. (Previously Presented) The pharmaceutical composition of Claim 11 wherein each R is, independently, hydrogen or linear or branched C_1-C_4-alkyl.

13. (Previously Presented) The pharmaceutical composition of Claim 12 wherein each R is, independently, hydrogen or methyl.

14. (Previously Presented) The pharmaceutical composition of Claim 13 wherein each R is hydrogen.

15. (Currently Amended) The pharmaceutical composition of Claim 1 wherein A is



of Formula II,

(II)

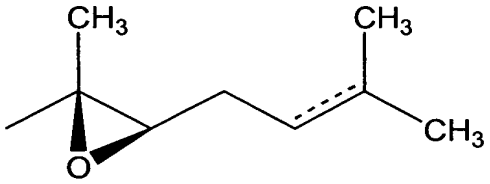
wherein

R_1 is hydrogen or alkoxy;

R_2 is hydrogen or hydroxy;

R_3 is hydrogen or alkyl; and

D is linear, cyclic, or branched alkyl or arylalkyl; or D is of the structure



16. (Previously Presented) The pharmaceutical composition of Claim 15 wherein R_1 is C_1-C_4-alkoxy.

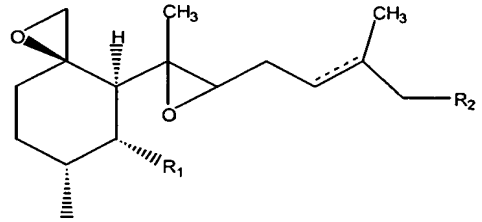
17. (Previously Presented) The pharmaceutical composition of Claim 16 wherein R_1 is methoxy.

18. (Previously Presented) The pharmaceutical composition of Claim 15 wherein R_3 is hydrogen or C_1-C_4-alkyl.

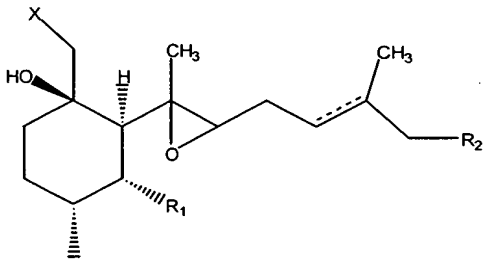
19. (Previously Presented) The pharmaceutical composition of Claim 18 wherein R_3 is methyl.

20. (Previously Presented) The pharmaceutical composition of Claim 15 wherein D is linear, branched or cyclic C_1-C_6-alkyl; or aryl-C_1-C_4-alkyl.

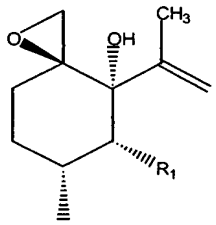
21. (Currently Amended) The pharmaceutical composition of Claim 1 wherein A is selected from the group consisting of



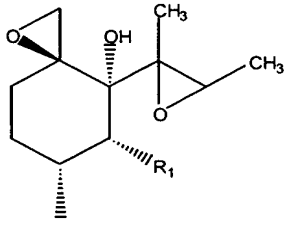
(IV)



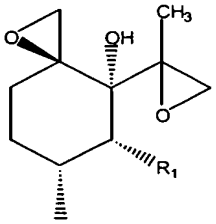
(V)



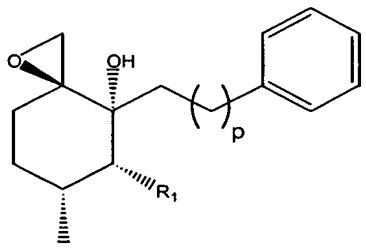
(VI)



(VII)



(VIII)

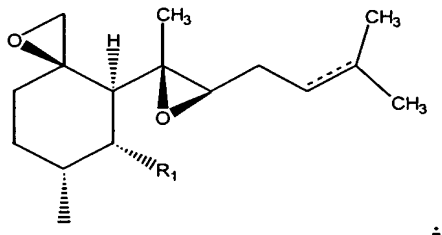


(IX)

and

wherein
p is an integer from 0 to 10;
R_1 is hydrogen, -OH or C_1-C_4-alkoxy;
X is a leaving group; and
R_2 is H, OH, amino, C_1-C_4-alkylamino or di(C_1-C_4-alkyl)amino~~)~~.

22. (Currently Amended) The pharmaceutical composition of Claim 21 wherein A is of the formula



23. (Previously Presented) The pharmaceutical composition of Claim 1 wherein P comprises from 1 to about 20 amino acid residues.

24. (Previously Presented) The pharmaceutical composition of Claim 23 wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

25. (Previously Presented) The pharmaceutical composition of Claim 24 wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

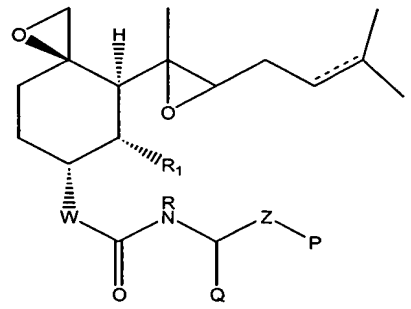
26. (Previously Presented) The pharmaceutical composition of Claim 25 wherein the matrix metalloprotease is MMP-2 or MMP-9.

27. (Previously Presented) The pharmaceutical composition of Claim 26 wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

28. (Currently Amended) The pharmaceutical composition of Claim 27 wherein P comprises the ~~a~~ sequence ~~selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His-(SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg-(SEQ ID NO:3); Pro-Gln-Gly-Ile-Ala-Gly-Trp~~

~~(SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5); Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:7); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15);~~ Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16); ~~Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23)~~.

29. (Previously Presented) A pharmaceutical composition comprising a compound of the formula



wherein

W is O or NR;

each R is, independently hydrogen or a C_1-C_4-alkyl;

Q is hydrogen; linear, branched or cyclic C_1-C_6-alkyl; or aryl;

R_1 is hydroxy, C_1-C_4-alkoxy or halogen;

Z is –C(O)- or C_1-C_4-alkylene;

P is NHR, OR, or a peptide comprising 1 to 100 amino acid residues attached to Z at the N-terminus; or

Z is alkylene-O or alkylene-NR; and

P is hydrogen or peptide comprising 1 to 100 amino acid residues attached to Z at the C-terminus;

or a pharmaceutically acceptable salt thereof; provided that when P is hydrogen, NHR or OR, Q is not hydrogen;

and a pharmaceutically acceptable carrier.

30. (Previously Presented) The pharmaceutical composition of Claim 29 wherein
W is O or NH;
Z is alkylene-O or alkylene-NH;
Q is isopropyl;
R_1 is methoxy; and
P comprises from 1 to 15 amino acid residues.

31. (Previously Presented) The pharmaceutical composition of Claim 30 wherein
W is O; and
P comprises 10 or fewer amino acid residues.

32. (Previously Presented) The pharmaceutical composition of Claim 29 wherein P comprises from 1 to about 20 amino acid residues.

33. (Previously Presented) The pharmaceutical composition of Claim 32 wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

34. (Previously Presented) The pharmaceutical composition of Claim 33 wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

35. (Previously Presented) The pharmaceutical composition of Claim 34 wherein the matrix metalloprotease is MMP-2 or MMP-9.

36. (Previously Presented The pharmaceutical composition of Claim 35 wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

37. (Currently Amended) The pharmaceutical composition of Claim 36 wherein P comprises the ~~a~~ sequence ~~selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His (SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg (SEQ ID NO:3); Pro-Gln-Gly-Ile-Ala-Gly-Trp (SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5); Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-~~

~~Trp-Ala-Arg (SEQ ID NO:7); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15);~~ Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16); ~~Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23)~~.

38. (Currently Amended) A pharmaceutical composition comprising a compound selected from the group consisting of

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-4-methyl-pentanoic acid methyl ester;

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-phenyl-acetic acid methyl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Hydroxymethyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)- 2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3,3-dimethyl-butyric acid methyl ester;

Cyclohexyl-2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-acetic acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-pentanoic acid methyl ester;

[1-(1-Carbamoyl-2-hydroxy-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl]-oxiranyl-1-oxa-spiro[2.5]oct-6-yl ester;

2-(3-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl}-ureido)-3-methyl-butyramide;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid;

(ID#31) N-Carbamoyl ~~(ID#31)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#30) N-Carbamoyl ~~(ID#30)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#32) N-Carbamoyl ~~(ID#32)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#40) N-Carbamoyl ~~(ID#40)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#39) N-Carbamoyl ~~(ID#39)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#26) N-Carbamoyl ~~(ID#26)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#27) N-Carbamoyl ~~(ID#27)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#24)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#36)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#37)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#38)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester; and

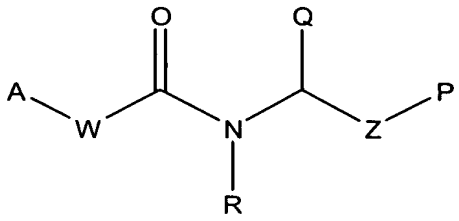
(ID#34)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

and a pharmaceutically acceptable carrier.

39. (Previously Presented) A method of treating an angiogenic-disease in a subject, comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising the compound of Formula I and a pharmaceutically acceptable carrier,

(I)

wherein



A is a MetAP-2 inhibitory core;
W is O or NR;
each R is, independently, hydrogen or alkyl;
Z is –C(O)- or -alkylene-C(O)-;

P is NHR, OR or a peptide consisting of one to about one hundred amino acid residues connected at the N-terminus to Z;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is –OR, Q is not hydrogen;

or Z is –alkylene-O- or –alkylene-N(R)-;

P is hydrogen or a peptide consisting of from one to about one hundred amino acid residues connected to Z at the carboxyl terminus;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is hydrogen, Q is not hydrogen; and a pharmaceutically acceptable salt thereof,

thereby treating the disease in the subject.

40. (Original) The method of claim 39, wherein said angiogenic disease is an autoimmune disease.

41. (Original) The method of claim 40, wherein said autoimmune disease is rheumatoid arthritis.

42. (Original) The method of claim 39, wherein said angiogenic disease is cancer.

43. (Original) The method of claim 39, wherein said subject is a human.

44. (Canceled)

45. (Previously Presented) The method of claim 39, wherein the pharmaceutical composition is administered to the subject intravenously.

46. (Previously Presented) The method of claim 39, wherein the pharmaceutical composition is administered to the subject intramuscularly.

47. (Previously Presented) The method of claim 39, wherein the pharmaceutical composition is administered to the subject orally.

48. (Currently Amended) The method of claim 39, wherein the compound of Formula I is selected from the group consisting of

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-4-methyl-pentanoic acid methyl ester;

{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-phenyl-acetic acid methyl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(1-Hydroxymethyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)- 2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3,3-dimethyl-butyric acid methyl ester;

Cyclohexyl-2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-acetic acid methyl ester;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-pentanoic acid methyl ester;

[1-(1-Carbamoyl-2-hydroxy-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl]-oxiranyl-1-oxa-spiro[2.5]oct-6-yl ester;

2-(3-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl}-ureido)-3-methyl-butyramide;

2-{(3*R*, 4*S*, 5*S*, 6*R*)-5-Methoxy-4-[(2*R*, 3*R*)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonylamino}-3-methyl-butyric acid;

(ID#31) N-Carbamoyl ~~(ID#31)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#30) N-Carbamoyl ~~(ID#30)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#32) N-Carbamoyl ~~(ID#32)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#40) N-Carbamoyl ~~(ID#40)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#39) N-Carbamoyl ~~(ID#39)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#26) N-Carbamoyl ~~(ID#26)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#27) N-Carbamoyl ~~(ID#27)~~ (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

(ID#24)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#36)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

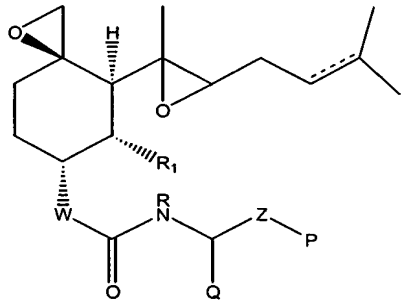
(ID#37)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester;

(ID#38)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester; and

(ID#34)-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R)2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl} amino-3-methyl-butanol) ester.

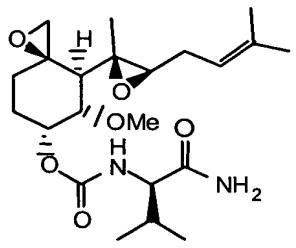
49. (Cancelled)

50. (Previously Presented) A pharmaceutical composition comprising a compound of the structure



and a pharmaceutically acceptable carrier, wherein
W is O;
each R is, independently hydrogen;
Q is a linear, branched or cyclic C_1-C_6-alkyl; or aryl;
R_1 is C_1-alkoxy;
Z is –C(O);
P is NHR;
or a pharmaceutically acceptable salt thereof.

51. (Currently Amended) A pharmaceutical composition comprising a compound of



the following structure and a pharmaceutically acceptable carrier.

52. (Previously Presented) A pharmaceutical composition comprising a compound of the structure (1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*,

3*R*) -2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester, and a pharmaceutically acceptable carrier.

53. (Previously Presented) The pharmaceutical composition of claim 1 formulated as a controlled release composition.

54. (Previously Presented) The composition of claim 53 wherein said controlled release formulation is a microcapsule.

55. (Previously Presented) The pharmaceutical composition of claim 52 formulated as a controlled release composition.

56. (Previously Presented) The composition of claim 55 wherein said controlled release formulation is a microcapsule.

57. (Previously Presented) The pharmaceutical composition of claim 1, further comprising a supplementary pharmaceutically active compound.

58. (Currently Amended) The pharmaceutical composition of claim 57, wherein said supplementary pharmaceutically active compound is selected from the group consisting of Taxol, Paclitaxel, Actinomycin D, an antidiabetic agent, Tolbutamide, heparin, and a sulfated cyclodextrin.

59. (Currently Amended) A method for treating an angiogenic disease in a subject comprising administering to said subject a compound comprising the structure (1-Carbamoyl-2-methyl-propyl)-carbamic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2*R*, 3*R*) -2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester.

60. (Previously Presented) The method of claim 59, wherein said compound is administered as a controlled release formulation.

61. (Previously Presented) The method of Claim 39 wherein the compound of Formula I is of the structure